UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

Fax Cover Sheet

Date: 20 Dec 2001

To: Jay Williams	**From:** Jon P. Weber, Ph.D.
Application/Control Number: 08/468,610	**Art Unit:** 1651
Fax No.: 703-836-2021	**Phone No.:** 703-308-4015
Voice No.: (703) 836-6620	**Return Fax No.:** 703-872-9306
Re:	**CC:**

☐ **Urgent** ☐ **For Review** ☐ **For Comment** ☐ **For Reply** ☒ **Per Your Request**

Comments:
Courtesy copy of Board Decision.

Number of pages 8 including this page

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SIMON C. BURTON, DAVID R.K. HARDING, NATHANIEL T. BECKER, BEN A BULTHUIS, and LANDON M. STEELE

Appeal No. 1999-1182
Application No. 08/468,610

HEARD: April 26, 2001

Before WILLIAM F. SMITH, ADAMS, and SCHEINER, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 5 and 7 through 23, all the claims in the application.

Claims 1 and 16 are representative of the subject matter on appeal and read as follows:

1. A resin-protein/peptide complex which comprises a resin and a target protein or peptide bound thereto wherein said resin comprises

a) a solid support matrix; and

b) selected ionizable ligand covalently attached to the matrix

wherein the ionizable ligand is selected such that the resin is electrostatically uncharged at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from the resin wherein desorption occurs by a change in the pH from the binding pH and further wherein about 50 percent or more of the target protein or peptide in an aqueous medium binds to the resin when the aqueous medium has either a high or low ionic strength.

16. A resin-protein/peptide complex which comprises a resin and a target protein or peptide bound thereto wherein said resin comprises

a) a solid support matrix having a selected ionizable functionality incorporated into the backbone thereof wherein the ionizable functionality is selected such that the resin is electrostatically uncharged at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from the resin wherein desorption occurs by a change in the pH from the binding pH; and

b) optionally a non-ionizable ligand covalently attached thereto,

wherein about 50 percent or more of the target protein or peptide in an aqueous medium binds to the resin when the aqueous medium has either a high or low ionic strength.

The references relied upon by the examiner are:

Jost et al. (Jost), "The Mode of Adsorption of Proteins to Aliphatic and Aromatic Amines Coupled to Cyanogen Bromide-Activated Agarose," Biochim. Biophys. Acta., Vol. 362, pp. 75-82 (1974)

Sasaki et al. (Sasaki 1979), "Hydrophobic-Ionic Chromatography, Its Application to Purification of Porcine Pancreas Enzymes," J. Biochem., Vol. 86, pp. 1537-48 (1979)

Sasaki et al. (Sasaki 1982), "Hydrophobic-Ionic Chromatography, Its Application to Microbial Glucose Oxidase, Hyaluronidase, Cholesterol Oxidase, and Cholesterol Esterase," J. Biochem, Vol. 91, pp. 1555-61 (1982)

Kasche et al. (Kasche), "Rapid Protein Purification Using Phenylbutylamine-Eupergit: A Novel Method for Large-Scale Procedures," J. Chromatography, Vol. 510, pp. 149-54 (1990)

Teichberg, "Affinity-Repulsion Chromatography," J. Chromatography, Vol. 510, pp. 49-57 (1990)

Claims 1 through 5 and 7 through 23 stand rejected under 35 U.S.C. § 103(a). As evidence of obviousness, the examiner relies upon Sasaki 1979 or Sasaki 1982 in view of Kasche, Teichberg, and Jost. We reverse.

Discussion

As set forth at page 7, lines 17-24 of specification:

> This invention relates to complexes of resins with proteins and peptides and methods for purifying target proteins or peptides using such resins. The resins described herein have ionizable functionality and a solid support matrix wherein the resin is electrostatically uncharged at the pH of target protein or peptide binding to the resin and electrostatically charged at the pH of desorption. Because of the lack of charge on the resin at the binding pH, difficulties and/or complexities associated with, for example, ion exchange resins can be avoided.

As can be seen, claim 1 is directed to one embodiment of the present invention wherein the resin comprises a solid support matrix and a selected ionizable ligand covalently attached to the matrix. Importantly, the "ionizable ligand is selected such that the resin is electrostatically uncharged at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from

the resin wherein desorption occurs by a change in the pH from the binding pH." Claim 16 is directed to a second embodiment of the present invention wherein the resin comprises a solid support matrix having a selected ionizable functionality incorporated into its backbone. The ionizable functionality is also "selected such that the resin is electrostatically uncharged at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from the resin wherein desorption occurs by a change in the pH from the binding pH."

The examiner's rejection is premised primarily upon the two Sasaki references. In describing these references at pages 4-6 of the Examiner's Answer, the examiner admits that each of the Sasaki references lacks "forming the complex with a resin that is uncharged between pH values of 5-9." Thus, the examiner admits that neither Sasaki reference describes a resin which meets the requirements of the claims on appeal.

Nor does the examiner assert in describing the Kasche, Teichberg, and Jost references on pages 6-7 of the Examiner's Answer that any one of these references teach a resin meeting the requirements of the claims on appeal. Rather, the examiner's position is stated at page 7 of the Examiner's Answer as follows:

> A person of ordinary skill in the art at the time the invention was made would have been motivated to form a complex between proteins and an uncharged ion exchange matrix at a pH value of between 5-9 from which the protein can be eluted by changing the pH value because Sasaki et al. (1979) and Sasaki et al. (1982) teach the general principle of binding

> proteins to uncharged ion exchange resins by hydrophobic effects and the subsequent elution of the bound proteins by a change in pH, and because of the generally recognized stability of proteins near physiological pH values of 5-9. The selection of pH values where the ion-exchange [sic] resin is uncharged is an arbitrary matter of experimental design choice.

Finally, the examiner makes clear his position at page 9 of the answer stating:

> The selection of a resin from among well-known chromatography resins for use in hydrophobic ionic chromatography where the resin is uncharged in the range of pH of 5-9 involves nothing more than routine experimentation to determine the titration curve of the resin. The selection of any given pH dependency for the resin will depend on the stability of the protein to be purified and the isoelectric point of the protein, parameters which are readily determined by the person of ordinary skill in the art or are already known to them. Sasaki et al. and Kasche et al. provide specific resins which are uncharged just outside the pH range claimed. Resins are known in the art which would be uncharged within the pH range of the scope of the claims.

By now it is well settled that obviousness must be based upon facts not generalities. In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968); In re Freed, 425 F.2d 785, 788, 165 USPQ 570, 571 (CCPA 1970). The examiner has asserted that "resins are known in the art which would be uncharged within the pH range of the scope of the claims." However, the examiner has not favored the record with any evidence in support of this assertion. As the record now stands, the prior art does not describe any resin which meets the requirements of the claims on appeal. In other words, the claimed resins are novel. If the examiner is aware of resins "known in the art which would be uncharged within the

pH range of the scope of the claims," it was incumbent upon him to provide evidence in the record documenting that fact. The examiner has not done so.

A conclusion of obviousness must be based upon the subject matter as a whole of a given claim. 35 U.S.C. § 103(a). Here, we only have the examiner's unsupported assertions that resins meeting the requirements of the claims on appeal are "known in the art." Absent evidence supporting those assertions, we cannot conclude that the subject matter of any claim as a whole would have been obvious to one of ordinary skill in the art.

The decision of the examiner is reversed.

REVERSED

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

Appeal No. 1999-1182
Application 08/468,610

Genencor International Inc.
925 Page Mill Road
Palto Alto, CA 94304

dem